

Ephedra and Its Application to Sport Performance: Another Concern for the Athletic Trainer?

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Objective: The ma huang herb, otherwise known as ephedra, has gained widespread popularity as an ergogenic supplement. With the sympathomimetic alkaloid ephedrine as its primary active ingredient, ma huang is marketed to reduce fatigue; increase strength, power, and speed; decrease reaction time; and improve body composition. Although numerous side effects have been associated with the use of ma huang, its popularity in athletes continues to grow. This review provides rationale for the ergogenic claims regarding ma huang and compares and contrasts those claims with data from scientifically controlled investigations.

Data Sources: MEDLINE and SPORT Discus were searched from 1970 to 2000 using the key words *ma huang*, *ephedra*, and *ephedrine* in combination with *humans*, *exercise*, *performance*, and *side effects*.

Data Synthesis: Ephedrine has been used alone or in com-

bination with other drugs as an effective weight-loss agent. The weight loss has been attributed to thermogenic and lipolytic effects which, in combination with the central nervous system stimulating effects, have also resulted in its use as an ergogenic aid. Most of the scientific data, however, do not support manufacturers' ergogenic claims, and numerous side effects have been associated with ephedrine use. Thus, the safety and efficacy of ma huang as an ergogenic supplement must be questioned.

Conclusions/Recommendations: It appears that the risks associated with the use of ma huang far outweigh any possible ergogenic benefits. Thus, it is extremely important that athletic trainers educate athletes on these issues so they can continue to perform at an optimum level in a safe and healthy manner.

Key Words: ma huang, ephedrine, ergogenic aid, performance enhancement

If you followed the 2000 Olympics in any way, you probably noticed a recurring headline. Regardless of the broken records and upset victories, the 2000 Olympics will always be known for the disqualifications and scandals surrounding the use of banned substances. One question that arose during the Games concerned the influence of nutritional supplement use on drug test results. The use of nutritional supplements for ergogenic benefit has gained increasing popularity over recent years and, in a report submitted after the Games, the World Anti-Doping Agency (WADA) concluded that there is widespread use, and possible abuse, of nutritional supplements in modern sport. Because they are considered natural and are available without a prescription, the misconception is that these supplements are all healthy and safe. Some of the more popular products are those marketed to either enhance energy or improve body composition. Many of these supplements contain the ma huang herb, otherwise known as ephedra (Table).

MA HUANG

Ephedrine

The plant species *Ephedra sinica*, *Ephedra equisetina*, and *Ephedra intermedia*, collectively known by their Chinese

name ma huang, are indigenous to Pakistan, China, and northwestern India.¹ For centuries, the dried stems of these plants have been used as a remedy for numerous medical conditions. In 1923, scientists discovered that the ma huang plant has 2 primary active ingredients: ephedrine (2-methylamino-1-phenyl-1-propanol) and pseudoephedrine, the same drugs commonly used in many nasal decongestant medications.^{1,2}

Ephedrine and pseudoephedrine are classified as sympathomimetic alkaloids because they directly stimulate the sympathetic, or "fight or flight," nervous system. These alkaloids are structurally similar to amphetamines and have direct alpha- and beta-agonistic properties and catecholamine-releasing actions.^{2,3} The alpha- and beta-sympathetic receptors are cell membrane receptors sensitive to epinephrine (adrenaline) and norepinephrine (noradrenaline) and are found on most cells throughout the body, including the cells of the heart, lungs, and surrounding blood vessels. Ephedrine alkaloids also function as indirect adrenoreceptor agonists.² Thus, they augment the availability and action of the natural neurotransmitter norepinephrine in the brain and in the heart.⁴ Unlike pseudoephedrine, ephedrine also mediates its effects via circulating epinephrine^{4,5} and is a bronchial dilator that has been used in the treatment of asthma.

Nutritional Supplements Containing Ma Huang

Supplement	Manufacturer	Ma Huang Content† (mg)	Caffeine Content (mg)
Xenadrine*	Cytodyne Technologies	20	200
BetaLean	EAS, Inc	20	150
Diet Stack	Metaform	16	66
Metacuts	Metaform	16.5	150
Metadrene	Metaform	18	100
Hydroxycut	MuscleTech Research & Develop.	20	200
Diet Fuel	Twin Laboratories, Inc	20	200
Metabolift Diet	Twin Laboratories, Inc	20	200
Ripped Fuel	Twin Laboratories, Inc	20	200

*Also contains 105 mg white willow bark extract (equivalent to 15 mg salicin) and 5 mg synephrine.

†Ephedrine alkaloid equivalent.

Pharmacokinetics

Ephedrine, pseudoephedrine, methylephedrine, norpseudoephedrine, and norephedrine have all been extracted from the ma huang plant. However, ephedrine and pseudoephedrine are the only 2 active components found consistently in ma huang products, with ephedrine being the predominant alkaloid.^{1,6} The other alkaloids are usually found only in small or trace amounts. For example, capsules containing 375 mg of ma huang have been found to contain an average of 4.84 mg (range, 3.8 to 5.9 mg), 1.22 mg (range, 0.77 to 1.82 mg), and 0.31 mg (range, 0.19 to 0.46 mg) of ephedrine, pseudoephedrine, and methylephedrine, respectively.¹ The levels of ephedrine alkaloids can also vary depending on the product and the ephedra species used.^{6,7} In an investigation of 9 commercially available supplements, Gurley et al⁶ observed considerable variability in both the ephedrine (range, 1.08 to 13.54 mg) and pseudoephedrine (range, 0.52 to 9.46 mg) contents. Two of the products contained measurable quantities of ephedrine only, which led the authors to speculate whether the product actually contained ma huang (as claimed on the label) or was instead spiked with synthetic ephedrine. Unfortunately, ma huang product labels usually indicate how much of the ephedra herb is present, but few identify the ephedrine alkaloid content.

Synthetic ephedrine is easily absorbed after oral administration, with peak plasma levels occurring within an hour of ingestion.⁸ Its plasma half-life is approximately 3 to 6 hours, which varies depending on urine pH.^{2,9} After absorption, ephedrine is excreted, primarily unchanged, in the urine: less than 10% is excreted as norephedrine. When ephedrine is ingested in the form of ma huang, the elimination kinetics are similar to those for synthetic ephedrine.^{1,7} Reports conflict, however, regarding absorption kinetics. Gurley et al⁷ investigated 3 brands of ma huang and observed absorption kinetics similar to those following ingestion of a 25-mg synthetic ephedrine capsule. In contrast, White et al¹ observed that it took longer for the ephedrine to reach peak levels in the plasma (approximately 4 hours) when ingested in the form of ma huang.

Ergogenic Claims

Because ephedrine is a sympathomimetic and a central nervous system stimulant, it is commonly used as an energy enhancer. Ma huang-containing products are marketed and used to improve aerobic performance and endurance, reduce fa-

tigue, increase alertness, improve reaction time, and even increase strength. These products are also marketed to body builders (and those simply concerned with cosmetic appearance) with the claim that they can improve body composition via thermogenic and lipolytic effects. The lipolytic effects have also led to the claim that ma huang can improve endurance via increased fat utilization and glycogen sparing during exercise. Because of this, it is very common to find ma huang products that also contain other thermogenic and lipolytic supplements, such as caffeine (usually found in the form of guarana).

Ephedrine and Caffeine

It has been suggested that the thermogenic effects of combining ephedrine and caffeine are synergistic (the effect of the 2 drugs combined is greater than their additive effects).^{10–12} Similar to ephedrine, caffeine has been suggested to have stimulating effects on the central nervous system (CNS) and energy metabolism.¹³ However, the primary reason for combining the 2 drugs is to potentiate the effects of the ephedrine.⁵ Ephedrine exerts its thermogenic effects via catecholamine release. The increased catecholamine release after ephedrine ingestion is subjected to negative feedback systems, which then tend to inhibit catecholamine release and actions. These negative feedback systems include adenosine and prostaglandin release in the synaptic junction and elevated phosphodiesterase enzyme activity, which results in degradation of cyclic adenosine monophosphate (cAMP). Caffeine interferes with this negative feedback mechanism by inhibiting both adenosine and phosphodiesterase activity and preventing degradation of cAMP.⁵ Aspirin has a similar effect via its inhibition of prostaglandin synthesis. Thus, it is conceivable that either of these mechanisms could potentiate the thermogenic effects of ephedrine. Because of this, some of the more popular weight-loss supplements on the market today combine ma huang (ephedrine), guarana (caffeine), and white willow bark extract (aspirin).

Effects on Performance

Many of the ergogenic claims associated with ephedrine originated from earlier studies investigating its anti-obesity and anorectic effects. Ephedrine and the combination of ephedrine and caffeine have been considered effective weight-loss agents,^{11,14–16} although not all studies support this claim.^{17–19} Originally, the observed weight loss was attributed solely to the appetite-suppressing effects of ephedrine²⁰; however, other mechanisms have more recently been suggested.^{14,17,19} In 3 weight-loss studies,^{11,15,16} body weight (as opposed to body composition) was the only variable assessed. Thus, it is unknown whether the weight loss was due to a reduction in fat mass or a loss of lean tissue and water mass. However, each of the authors suggested that increased energy expenditure (and primarily fat metabolism) accounted for most of the weight loss.

Thermogenesis and Lipolysis

The measurement of oxygen consumption ($\dot{V}O_2$) is the primary index and documented evidence of a person's aerobic metabolism and energy expenditure. Thus, thermogenic claims associated with ephedrine have been supported, as increases

in resting $\dot{V}O_2$ have been observed after both acute and chronic ephedrine ingestion.¹⁴ Similarly, ephedrine and combined ephedrine and caffeine have been observed to partially prevent the usual fall in resting metabolic rate during a calorie-restricted diet.^{17–19} However, the higher metabolic rates observed in these studies were not always associated with weight loss.^{17,19} There is also support for lipolytic claims, as significant increases in both fat oxidation and fat loss have been observed when ephedrine is administered in combination with caffeine.¹⁷ In contrast, however, ephedrine ingestion alone failed to produce such changes.¹⁴ Only clinically obese individuals were used as subjects in these investigations; thus, it is likely that the subjects may have had deficient metabolic rates or fat metabolism or both. Unfortunately, it is common practice for supplement manufacturers to take results from deficiency studies and generalize them to young, healthy, athletic individuals when advertising their products. Those of us in the research community know that this cannot and should not be done.

Exercise Performance

While the research concerning ephedrine and performance in an athletic population is limited, most investigations do not support ergogenic claims.^{21–25} As mentioned previously, $\dot{V}O_2$ is a primary measure of aerobic performance and, although ephedrine ingestion has been observed to increase resting $\dot{V}O_2$ and fat oxidation in healthy individuals,^{26,27} these changes have not been observed during exercise.^{12,22,24,28} Similar observations have been made after pseudoephedrine ingestion, as no differences in $\dot{V}O_2$ occurred in comparison with placebo conditions during exercise.^{25,29} As with $\dot{V}O_2$ and fat oxidation, a number of other performance measures have been unaffected by supplementation.^{23–25} Sidney and Lefcoe²⁴ administered 24 mg of ephedrine and found no improvements in muscle strength, endurance, or power; lung function; reaction time; hand-eye coordination; anaerobic capacity or speed; cardiorespiratory endurance; ratings of perceived exertion; or recovery. Similarly, Gillies et al²³ reported that a single 120-mg dose of pseudoephedrine had no effect on 40-km cycling time, maximal muscle force, or muscle endurance during repeated isometric contractions. More recently, Swain et al²⁵ administered pseudoephedrine (1 and 2 mg/kg) to trained cyclists and found no changes in ratings of perceived exertion or time to exhaustion.

One group of researchers, however, has observed performance changes when combining ephedrine with caffeine. Bell et al¹² observed that the combination significantly increased cycling time to exhaustion by 38% over a placebo condition, while ephedrine and caffeine given separately failed to provide such an effect. In another study, the combination of ephedrine and caffeine improved cycling time to exhaustion by 64% over a placebo condition.²⁸ In both studies, ratings of perceived exertion were significantly lower after supplementation, but heart rate was significantly elevated as well. The authors attributed the improvement to CNS stimulation, as no changes were observed for $\dot{V}O_2$, carbon dioxide production, or fat oxidation. It is important to note that one would have to double the serving size of typical sport supplements containing both ephedrine and caffeine (Table) to achieve the doses used in these 2 studies. More recently, Bell and Jacobs³⁰ administered 75 mg of ephedrine with 375 mg of caffeine and observed a slight (5%) but significant improvement in running time during a Canadian Forces Warrior Test (3.2 km run while wearing

field gear). Unfortunately, the literature supporting the ergogenic claims associated with ephedrine in a healthy population appears to be limited to just one group of researchers. Negative side effects were commonly observed during these investigations and others involving both healthy and obese individuals.^{7,11,12,14–18,21,25,26,28}

Side Effects

The spectrum of adverse health events associated with the use of ephedrine-containing products cannot be overlooked. The Food and Drug Administration (FDA) has received more than 1000 reports of adverse effects (including deaths) in persons ingesting nutritional supplements containing ephedrine and associated alkaloids.³¹ These side effects vary and do not always depend on the dose consumed.³² Although the occurrence of side effects was likely the result of misuse in many cases, such side effects have been regularly observed in subjects involved in clinical trials in which the dosages were controlled.^{7,11,12,14–18,21,25,26,28}

Some of the minor side effects associated with ephedrine include tremors, palpitations, headache, restlessness, anxiety, and insomnia.^{9,17,25,32} Because of its direct sympathomimetic effects, ephedrine can increase heart rate, contractility, cardiac output, and peripheral resistance. Thus, increases in both heart rate and blood pressure are common observations after ephedrine ingestion.^{10,12,21,23–25,32} This is also true after ma huang ingestion, as significant increases in heart rate and blood pressure have been observed.^{1,7} Although these effects are not serious in most users, the consequences can be severe in those with underlying heart disease, hypertension, or diabetes and those sensitive to ephedrine.⁶ The more serious side effects include seizures, severe hypertension, arrhythmias, psychosis, hepatitis, stroke, myocardial injury, and intracranial hemorrhage.^{3,32–38} The adverse effects do not always depend on the dose consumed, as serious problems can occur in susceptible persons with use of low dosages.^{9,32} Furthermore, the toxicity of sympathomimetic agents is exacerbated by physical exercise, dehydration, and increases in body temperature,²² which are all commonly experienced during athletic training.

Although few in number, cases of fatal intoxication after ephedrine ingestion have been reported.^{8,32} In instances of ephedrine overdose, cardiovascular and CNS stimulant effects predominate. The most common causes of death are myocardial infarction and cerebrovascular accident.³² The recent death of a young, apparently healthy male college student brought attention to the possible dangers associated with ma huang-containing products. The individual regularly consumed a product containing ephedrine and caffeine known as Ripped Fuel (Twin Laboratories Inc, Ronkonkoma, NY).⁴ The official autopsy report and death certificate read “patchy myocardial necrosis associated with ephedrine toxicity from protein drink containing ma huang extract.” The blood and urine ephedrine levels suggested that the death was not caused by an acute poisoning but was the result of prolonged use.

CONCLUSIONS

Over-the-counter availability and unrestrained self-medication with products containing ma huang create a heightened potential for serious side effects. Unfortunately, most companies that manufacture and sell nutritional supplements are prof-

it driven and often use misleading advertising. One of the primary concerns is that manufacturers are not required to list the ingredients on the labels of natural supplements; thus, the consumer does not always know the true contents of the product. One product labeled “no side effects” was found to contain 45 mg of ephedrine and 20 mg of caffeine in a single tablet, despite the fact that it listed Chinese ginseng as the only ingredient.³² The label also instructed users to take 5 tablets, which represents a total ephedrine dosage of approximately 11 times the usual recommended over-the-counter dosage.

Recent changes by the FDA regarding the definition of a nutritional supplement have allowed a wide variety of products to be considered as such, and, although the term *natural* implies it, they are not always healthy and safe. Because of widespread reports of adverse events associated with ma huang use, the FDA has proposed to limit the allowed dose of ephedrine to 8 mg per serving or 24 mg per day.³¹ Furthermore, manufacturers would be required to state on the label that the product is not to be used for more than 7 days. At this time, however, these changes are still being assessed and no definitive decisions have been made. Both the International Olympic Committee and the National Collegiate Athletics Association have banned ephedrine and ephedrine alkaloids.

Whenever an athlete is considering using ma huang or any ergogenic supplement, two questions must be asked: is it safe and does it work? Ephedrine appears to be an effective CNS stimulant with thermogenic and lipolytic effects. However, its ergogenic advantages are highly debatable and the dangers associated with its immediate and prolonged use are well documented. Thus, it appears that the risks far outweigh the benefits. The key to performance is a healthy diet and a well-developed training program: there is no “quick fix” or “shortcut to success.” As allied health professionals, athletic trainers must be able to educate athletes on these issues so they continue to perform at optimal levels in a safe and healthy manner.

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